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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/746,921	12/22/2000	Kevin J. Thorne	2265-15	2764

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EXAMINER	
LEITH, PATRICIA A	
ART UNIT	PAPER NUMBER
1655	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/746,921	THORNE ET AL.	
	Examiner	Art Unit	
	Patricia Leith	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/20/06*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8-10,32,33,35-37,44 and 48-50* is/are pending in the application.

4a) Of the above claim(s) *9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 8, 10, 32-33 35-37, 44 and 48-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 8-10, 32-33 35-37, 44 and 48-50 are pending in the application.

Claim 9 has been withdrawn from further consideration on the merits as it is directed toward a non-elected invention.

Claims 1, 8, 10, 32-33, 35-37, 44 and 48-50 were examined on their merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a previous Office Action.

Applicant's amendment has overcome the previous rejections; hence, Applicant's arguments pertaining to the previous rejections are found persuasive with regard to the newly amended claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 8, 10, 32-33, 35-37, 44 and 48-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 35 newly recite that both Type I and Type II collagen are present in the bone growth composition. This is considered New matter because it cannot be found in the Instant disclosure as filed where Applicant contemplated the use of these two types of collagen together. Because claims 8, 10, 32-33, 36-37, 44 and 48-50 are directly or indirectly dependant upon claim 1, claims 8, 10, 32-33, 36-37, 44 and 48-50 necessarily include all of the limitations of claim 1 and thus also contain New matter and are properly rejected under this statute.

Applicant is asked to delete the New matter, or to amend the claims accordingly to overcome this rejection.

Rejections under 35 USC 102 and 103 not reinstated in this Office Action were removed due to Applicant's amendments to the claims. Applicant's arguments

pertaining to the previous rejections are rendered moot in light of the removal of those rejections.

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 8, 10, 32-33, 35-37, 44 and 48-50 rejected under 35 U.S.C. 103(a) as being unpatentable over Clarke et al. (1993) in view of Constantz (US 5,047,031) in view of Piez et al. (US 4,795,467).

Clarke et al. (1993) explained that "Osteogenic bioactive materials stimulate bone regrowth, and are generally composed of natural materials". Clarke et al. disclosed a bone material made solely of brushite, Ser P bone growth protein and Type I rabbit collagen prepared, in part, *via* calcium phosphate mineralization of decalcified rabbit femur (collagen type I) (see entire reference, especially Experimental procedure pp. 107-108). It is clear that hydroxyapatite solution was used as the mineralization component, however, after the bone material had completely set "the precipitation of brushite was verified" (see p. 108, col. 2, 'Results and discussion').

Clark did not teach the incorporation of bovine types I and III (atelopeptide-type) collagen, or wherein the collagen was crosslinked or the particular amounts of constituents as claimed.

Constantz (US 5,047,031) discloses a bone cement composition which advantageously employs calcium phosphate compositions such as brushite (calcium hydrogen phosphate dihydrate) (column 1) , collagen such as Type I collagen and bone proteins such as bone morphogenic proteins (col. 6, lines 3-22).

Piez et al. (US 4,795,467) teach that:

"The general notion of using mixtures or combinations of collagen protein and bone materials in effecting hard tissue repair has been known for some time. As bone itself is comprised of these minerals, along with collagen, it seemed promising to utilize this combination....performance is improved over that resulting from use of collagen from, for example bovine or porcine (col. 1, lines 16-39),

and

Native collagen consists mainly of a triple helical structure containing repeating triplet sequences composed of glycine linked to two additional amino acids, commonly proline and hydroxyproline. *Native collagen contains regions at each end which do not have the triplet glycine sequence, and thus do not form helices. These regions are thought to be responsible for the immunogenicity associated with most collagen preparations, and the immunogenicity can be mitigated by the removal of these regions to produce "atelopeptide" collagen.* This can be accomplished by digestion with proteolytic enzymes, such as trypsin and pepsin. The non-helical telopeptide regions are also responsible for natively occurring cross-linking, and

atelopeptide collagen must be cross-linked artificially if cross-linking is desired. (col. 3, lines 29-44) emphasis added

collagen preparations may differ from each other by virtue of their initial compositions which is a function of their origin, or by virtue of their modes of preparation. Collagen derived from bone, for example, contains exclusively Type I collagen; while collagen derived from skin also contains Type III. Also, the process of preparation may or may not remove the telopeptides. Thus both unaltered and "atelopeptide" collagen are possible. Cross-linking may be effected deliberately or accidentally. *Sterilization by .gamma.-irradiation or by high heat may result in cross-linking without control of extent or nature and results in partial degradation of the triple helix; deliberate cross-linking may be carried out by a variety of means, including treatment with glutaraldehyde.* Differences arising from perhaps more subtle causes are perhaps the result of variations in the details of the preparation procedure. For example, the collagen may be solubilized and reprecipitated, or may simply be finely divided and kept in suspension. When the solubilized material is reaggregated, the aggregation may be done in ways so as to form non-specifically bonded solids, or the collagen may be reconstituted into fibers which simulate the native form. Also, of course, the degree of purity may vary. (col. 3, line 59 – col. 4 line 15) emphasis added

Piez et al. specifically teach a bone material comprising calcium phosphate and atelopeptide crosslinked collagen, and suggest the preferred use of bovine or ovine collagen , and wherein the collagen is type I or type III (see entire reference, especially claims, col. 3, lines 29-58 and col. 1, lines 16-38). It is deemed that wherein Piez et al. teach wherein the collagen is treated with 'high heat' (see citation, *supra*), that this description fits the term 'dehydrothermally' as dehydrothermal crosslinking occurs because of heat treatment of the collagen. Piez et al. further teach that crosslinking of the collagen in the bone composition is advantageous because it improves the compressive strength of the bone material (see Abstract).

One of ordinary skill in the art would have been motivated to modify the bone composition of Clarke which contained brushite (calcium hydrogen phosphate dihydrate) and collagen type I (rabbit) to include crosslinked bovine atelopeptide collagens I and III because both of these types of collagens would have been a suitable replacement for the type I collagen disclosed by Clarke and because Piez et al. clearly taught that the use of bovine and porcine collagens were better suited for bone compositions intended for human use due to their reduced immunogenicity. One of ordinary skill in the art would have been motivated to crosslink the collagen in order to afford the bone composition improved compressive strength. The ordinary artisan would have had a reasonable expectation as such because Piez et al. specifically taught that crosslinked collagen (*via* dehydrothermalization or other means suitable for

crosslinking collagen as also taught by Piez et al.) afforded the bone composition better compressive strength. The ordinary artisan would have had a reasonable expectation that the use of bovine atelopeptide collagens I and II would be more advantageous than the use of the rabbit type –1 collagen used by Clarke because the bovine atelopeptide collagens I and II would be more easily accepted by the human immune system.

One of ordinary skill in the art would have been motivated to substitute the Ser P bone proteins for a BMPs in the bone composition disclosed by Clark et al. because the addition or substitution of such bone proteins would have increased the formation of endogenous bone upon implantation. It is clear from Constanz that BMP's (bone proteins) are routinely used with bone compositions comprising calcium phosphates (such as brushite) and collagens in order to enhance the formation of endogenous bone. Therefore, one of ordinary skill in the art would have had a reasonable expectation that the addition of autologous growth factors such as BMP's would have had a positive effect on bone repair when combined with a bone composition including brushite and crosslinked bovine collagens I and III.

Although the prior art does not specifically teach the amounts of constituents as Instantly claimed, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal concentrations of components because concentration is an art-recognized result-effective variable which would have been routinely determined and optimized in the

pharmaceutical art. Further, if there are any differences between Applicant's claimed method and that suggested by the teaching of the prior art, the differences would be appear minor in nature. Although the prior art do not teach all the various permutations of concentration ranges as claimed , it would be conventional and within the skill of the art to identify the optional concentrations of a given ingredient because Contstanz clearly taught that these parameters were to be suitably varied in order to formulate desired bone construction (see col. 6, line 26-col.7, line 3. Thus, the selection of appropriate concentration of ingredients to stabilize bone cement compositions for the intended purpose of replacing natural bone (e.g., teeth) is conventional and within the skill in the art.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on Monday - Friday 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Patricia Leith
Primary Examiner
Art Unit 1655

January 31, 2007